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TOBACCO INDUSTRY RESEARCH COMMITTEE
350 FIFTH AVENUE NEW YORK 1, N. Y.

Application For Research Grant

Arbitrary

Date: October 15, 1954

1. Name of Investigator: Aldo A. Luisada, M.D.

2. Title: Associate Professor of Medicine of The Chicago Medical School and Director, Division of Cardiology, The Chicago Medical School.

3. Institution: The Chicago Medical School - Assistant Professor of Pharmacology.
& Address: 710 South Wolcott Avenue of consultant.
Chicago 12, Illinois

4. Project or Subject: Action of Products of Combustion of Tobacco Leaves on the Circulation

5. Detailed Plan of Procedure (Use reverse side if additional space is needed):

has it? cause + effect

It has been proven that cigarette smokers have a higher percentage of coronary heart disease than either non-smokers or pipe or cigar smokers. This would point out to a specific action of products which are contained in the smoke of cigarettes and not to a general effect of nicotine.

Why?

We would like to study on humans and animals the effect of several alkaloids which have been demonstrated in the smoke of cigarettes. The average leaves of Kentucky tobacco contains about 4% of alkaloids. Following their extraction, 95% of the total alkaloid extract is made of nicotine while 2% is a mixture of nor-nicotine and l-anabasine; 0.5% is nicotinine; 0.1% is nicotelline; about 10 other, less well known, alkaloids make up the balance. From what is known, l-anabasine is the most toxic of these alkaloids.

Tobacco smoke contains some alkaloids of the tobacco leaf (mostly nicotine) and eight other alkaloids which are the result of the process of combustion. Only myosmine has been studied among the latter.

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Signature: /s/ page
Director of Project
Aldo A. Luisada, M.D.

Business Officer of the Institution

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how

We plan to isolate chemically the various alkaloids of cigarette smoke and test them in the following ways:

- (1) Human experiments on volunteers. Electrocardiograms, ballistocardiograms, and plethysmograms before and after smoking the first cigarette after a period of 3 days abstinence from smoking.

(This would give a standard type of reaction which could be compared with those of experimental animals).

- (2) Comparison of the intravenous and intrabronchial (aerosol) administration of the various fractions of cigarette smoke in dogs.

- (a) Intact, anesthetized animals (electrocardiogram, blood pressure, ballistocardiogram, plethysmogram).

- (b) Heart-lung preparation (electrocardiogram, blood pressure).

accumulation to meeting

too indefinite to make any production?

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6. Budget Plan:

350 FIFTH AVENUE

Salaries

7,400.00

Expendable Supplies

1,500.00

Applied Permanent Equipment

500.00

Overhead

940.00

Other

Total \$10,340.00

Date October 25, 1954 Total \$10,354

7. Anticipated Duration of Work: Two years

8. Facilities and Staff Available: The staff of the Division of Cardiology, including the Director and 6 full-time Research Assistants, will take part to this study. The Chemical extraction will be done by Dr. J. Sicé, in the Division of Oncology of this School. Dr. Sicé, Assistant Professor of Pharmacology, will also be available in the capacity of consultant.

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The Technical facilities of the Division of Cardiology (including electrocardiographs, phonocardiograph, ballistocardiograph, plethysmograph, and pressure recorders) are available.

9. Additional Requirements:

10. Additional Information (Including relation of work to other projects and other sources of supply):

If any specific alkaloid is proven to be the cause of coronary or peripheral vasoconstriction, it is anticipated that different methods of preparation of the tobacco leaves might exclude it from the finished product, thereby removing the main cause of morbidity in regard to the heart and vessels. It is also possible that certain drugs may act as antidotes or antagonist and might be mixed with the tobacco, thereby neutralizing the noxious effects.

[illegible]

...while certain rare alkaloids of the tobacco are mostly absent, and eight other alkaloids which are the result of the presence of ... Only nicotine has been studied among the latter.

Signature:

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Director of Project

Aldo A. Luisada, M.D.

/s/

Business Officer of the Institution

Henry E. Mitchell

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